Alerts, Notices, and Case Reports

Cocaine-Induced Intestinal Ischemia

MUHAMMAD A. WATTOO, MD
OLUSOLA OSUNDEKO, MD
Philadelphia, Pennsylvania

COCAINE, AN ALKALOID derived from the *Erythroxylon coca* plant, remains a popular recreational drug.[1] Although its recreational use has decreased, the number of hard-core regular users remains unchanged at 476,000 according to the 1993 National Institute on Drug Abuse Household Survey.[2] Cocaine-related complications are, therefore, of clinical importance. Bowel ischemia due to cocaine use is probably more common than is reported, but it may be overlooked because its presentation is similar to other acute abdominal conditions. A direct causal relationship between cocaine use and bowel ischemia is difficult to prove. Nevertheless, the patients described in published reports so far had been relatively young, had a positive urine toxicology screen for cocaine, and had no previous history of atherosclerosis. We report a case of acute small bowel ischemia in the oldest patient after smoking crack cocaine.

Report of a Case

The patient, a 50-year-old man who smoked cigarettes and crack cocaine regularly, presented to the emergency department with a three-day history of abdominal pain, nausea, vomiting, and poor urine output after a binge of alcohol and cocaine use. The abdominal pain was sudden in onset, severe in intensity, and located mainly in the lower abdomen. The pain was made worse by oral intake and had no relieving factors. There was no history of fever, chills, chest pain, back pain, shortness of breath, or seizures. He had been unable to eat or drink for three days because of the pain.

On examination, the patient was awake and alert but looked uncomfortable. Apart from tachycardia (115 beats per minute), he had normal vital signs. He was clinically dehydrated. He had diffuse tenderness in the lower abdomen with guarding in his right lower quadrant, but no rebound was elicited at this stage. Bowel sounds were markedly diminished, and a rectal examination showed occult blood in the stool. Pertinent laboratory data included the following values: a leukocyte count of 30×10^9 per liter (30,000 per µl) with a leftward shift; hemoglobin level, 185 grams per liter (18.5 grams per dl); hematocrit, 0.55 (55%); platelet count, 300×10^9 per liter (300,000 per µl); serum bicarbonate, 19 mmol per liter; blood urea nitrogen, 16.4 mmol per liter (46 mg per dl); creatinine, 582 µmol per liter (6.6 mg per dl); phosphate, 3.13 mmol per liter (9.7 mg per dl; normal, 0.80–1.55 mmol per liter); and anion gap, 28. Other laboratory results were a creatine kinase level of greater than 16,000 units per liter (normal, 20–315); lactate dehydrogenase level, 9,282 units per liter (normal, 111–217); aspartate aminotransferase, 1,996 units per liter (normal, 3–26); alanine aminotransferase, 580 units per liter (normal, 5–30); alkaline phosphatase, 144 units per liter (normal, 25–128); amylase, 270 units per liter (normal, 30–120); and lipase, 144 units per liter (normal, 0–200). A urinalysis revealed 1-plus ketones, 3-plus blood and protein, 40 to 50 white blood cells per high-powered field, and few bacteria. The findings of urine microscopy were consistent with acute tubular necrosis.

Abdominal roentgenogram showed only a nonspecific bowel gas pattern. Computed tomography showed abdominal ascites and fluid collection or inflammatory changes (or both) in the right lower quadrant. The patient was admitted to the intensive care unit and was given fluid resuscitation and antibiotics. After a few hours, the patient became febrile, his abdominal pain worsened, and he had abdominal distension, generalized rebound tenderness, and absent bowel sounds. The patient underwent an exploratory laparotomy that revealed gangrenous distal small bowel, including the distal ileum. A 75-cm segment of the nonviable bowel was resected, and an end-to-end anastomosis was done. Microscopic examination of the specimen of resected bowel revealed acute ischemic necrosis of the small bowel wall. There was no thrombus, embolus, or atherosclerosis. The patient received hemodialysis, his renal function improved gradually, and he was subsequently discharged.

Discussion

We searched MEDLINE for the literature on cocaine-induced bowel ischemia.[3–17] The review excluded those who swallowed condom-filled cocaine packets with the intention of smuggling the drug—the so-called body packers. There were 18 cases to date, with most patients in their third or fourth decade of life. Our patient was the oldest at 50 years of age. There was nearly a 2:1 ratio of women to men. No method of administering cocaine is safe. Apart from two patients whose route of administration was unknown, most patients either smoked crack cocaine or injected it intravenously. Most cases involved ischemia of the small rather than the large bowel, and two thirds of the patients recovered, usually with surgical management (Table 1).

(Wattoo MA, Osundeko O. Cocaine-induced intestinal ischemia. West J Med 1999; 170:47–49)

From the Department of Internal Medicine, University of Pennsylvania Health System, Presbyterian Medical Center, Philadelphia, Pennsylvania.

Reprint requests to Olusola Osundeko, MD, Department of Internal Medicine, University of Pennsylvania Health System, Presbyterian Medical Center, 39th and Market Sts, Philadelphia, PA 19106 (e-mail: Olusola@yahoo.com).

TABLE 1.—*Reported Cases of Cocaine-Induced Bowel Ischemia**

Reference	Age, y	Sex	Route	Site of Ischemia	Outcome
This report	50	M	Smoked crack	Small bowel	Survived
Sudhakar et al, 1997[3]	35	F	Unknown	Small bowel	Died
Sudhakar et al, 1997[3]	32	F	IV	Small bowel	Survived
Boutros et al, 1997[4]	36	F	Smoked crack	Large bowel	Survived
Myers et al, 1996[5]	29	F	IV, smoked crack	Celiac artery thrombosis, mesenteric ischemia	Survived
Myers et al, 1996[5]	35	F	IV	Distal ileum, cecum	Survived
Jawahar et al, 1995[6]	31	F	Intranasal	Small bowel	Died
Yang et al, 1991[7]	26	F	Smoked crack	Large bowel	Survived
Freudenberger et al, 1990[8]	38	M	IV	Small bowel	Died
Mizrahi et al, 1988[9]	27	M	Intranasal	Small bowel	Survived
Endress et al, 1992[10]	30	F	Smoked crack	Small bowel	Survived
Hazanas et al, 1993[11]	23	F	Oral	Large bowel	Died
Hon et al, 1990[12]	37	F	Smoked crack	Small bowel	Survived
Garfia et al, 1990[13]	24	M	Not specified	Small bowel	Died
Martin, 1991[14]	30	M	Intranasal	Bowel	Survived
Brown et al, 1994[15]	47	M	IV	Large bowel	Survived
Fishel et al, 1985[16]	37	M	Smoked crack	Cecum and ascending colon	Survived
Nalbandian et al, 1985[17]	29	F	Oral	Small bowel	Survived
Nalbandian et al, 1985[17]	26	F	Oral	Distal small bowel and proximal colon	Died

*IV = intravenous injection

In keeping with previously described patients, our patient had no history of predisposing factors that make other causes of bowel ischemia likely. An additional factor may be cigarette smoking, a common finding among those who use cocaine. The combined use of cocaine and smoking has a probable additive effect on coronary artery vasoconstriction.[18] This may be applicable to other vessels elsewhere in the body, including mesenteric vessels. Our patient had been smoking for many years and was a current smoker at the time of his illness.

This patient had rhabdomyolysis that resolved with medical treatment. We had expected rhabdomyolysis to be a common complication among patients with bowel ischemia because ischemia is its most frequent cause.[19] Rhabdomyolysis, however, may be rare or underreported because there is only one reported case linking it to bowel ischemia.[8] We suggest that rhabdomyolysis should be screened for in all these patients because it may cause acute renal failure.[19]

Cocaine is a well-known central nervous stimulant, local anesthetic, and pyrogenic agent. Several mechanisms have been proposed to explain how cocaine causes bowel ischemia. It potentiates the normal adrenergic response by blocking the reuptake of presynaptic monoamine neurotransmitters.[20] Mesenteric vessels contain many α-adrenergic receptors.[21] Stimulation of these receptors causes intense vasoconstriction, leading to reduced blood flow and ischemia. Cocaine also has a direct vasoconstrictive effect by enhancing calcium flux across the endothelial membrane.[22] Some investigators have suggested that cocaine has a direct toxic effect on the gut mucosa.[23] Cocaine displaces the transmitter from the axonal membrane, thereby inducing a sympathomimetic response.[24] Thrombus formation and platelet aggregation are enhanced following cocaine administration.[25] Cocaine also decreases fibrinolytic activity by stimulating plasminogen activator inhibitor activity.[26] Some or all of these effects of cocaine may explain the increased susceptibility of the bowel to ischemia in patients who abuse this drug.

This report highlights the importance of including cocaine use in the differential diagnosis of acute abdomen in all patients. That our patient was 50 years old suggests that probably no age barriers to drug abuse exist. Many cases may go unrecognized for different reasons. Some patients may be reluctant to admit to cocaine use, drug testing is not uniform, and dose-related complications are not consistent.[27]

REFERENCES

1. Catterall W, Mackie K. Local anesthetics. In Hardman JG, Limbird LE, Molinoff PB, Ruddon RW, Gilman AG (Eds): The Pharmacological Basis of Therapeutics. 9th ed. New York, McGraw-Hill, 1996, pp 331–347

2. Substance Abuse and Mental Health Services Administration, Office of Applied Statistics. National Institute of Drug Abuse Household Survey, 1993. Rockville, Md, National Institute on Drug Abuse, US Dept of Health and Human Services, 1994

3. Sudhakar CB, Al-Hakeem M, MacArthur JD, Sumpio BE. Mesenteric ischemia secondary to cocaine abuse: case reports and literature review. Am J Gastroenterol 1997; 92:1053–1054

4. Boutros HH, Pautler S, Chakrabarti S. Cocaine-induced ischemic colitis with small-vessel thrombosis of colon and gallbladder. J Clin Gastroenterol 1997; 24:49–53

5. Myers SI, Clagett GP, Valentine RJ, Hansen ME, Aditi A, Arun C. Chronic intestinal ischemia caused by intravenous cocaine use: report of two cases and review of the literature. J Vasc Surg 1996; 23:724–729

6. Jawahar D, Leo PJ, Anandarao N, Pachter BR. Cocaine-associated intestinal gangrene in a pregnant woman. Am J Emerg Med 1997; 15:510–512

7. Yang RD, Han MW, McCarthy JH. Ischemic colitis in a crack abuser. Dig Dis Sci 1991; 36:238–240

8. Freudenberger RS, Capell MS, Hutt DA. Intestinal infarction after intravenous cocaine administration. Ann Intern Med 1990; 113:715–716

9. Mizrahi S, Laor D, Stamier B. Intestinal ischemia induced by cocaine abuse (Letter). Arch Surg 1988; 123:394

10. Endress C, Gary DGK, Wollschlaeger G. Bowel ischemia and perforation after cocaine use. AJR Am J Roentgenol 1992; 159:73–75

11. Hazanas FH, Torres CP, Delgado FI. Multiorgan failure and intestinal ischemia after cocaine intoxication (Letter). Intensive Care Med 1993; 19:239–240

12. Hon DC, Salloum LJ, Hardy HW III, Barone JE. Crack-induced enteric ischemia. N J Med 1990; 87:1001–1002

13. Garfia A, Valverde JL, Borondo JC, Candenas I, Lucena J. Vascular lesions in intestinal ischemia induced by cocaine-alcohol abuse: report of a fatal case due to overdose. J Forensic Sci 1990; 35:740–745

14. Martin TJ. Cocaine-induced mesenteric ischemia. N C Med J 1991; 52:429–430

15. Brown DN, Rosenholtz MJ, Marshall JB. Ischemia colitis related to cocaine abuse. Am J Gastroenterol 1994; 89:1558–1561

16. Fishel R, Hamamato G, Barbul A. Cocaine colitis: is this a new syndrome? Dis Colon Rectum 1985; 28:264–266

17. Nalbandian H, Sheth N, Dietrich R, Georgiou J. Intestinal ischemia caused by cocaine ingestion: report of two cases. Surgery 1985; 97:374–376

18. Moliterno DJ, Willard JE, Lange RA, Negus BH, Boehrer JD, Glamann DB, et al. Coronary-artery vasoconstriction induced by cocaine, cigarette smoking, or both. N Engl J Med 1994; 330:454–459

19. Veenstra J, Smit WM, Krediet RT, Arisz L. Relationship between elevated creatine phosphokinase and the clinical spectrum of rhabdomyolysis. Nephrol Dial Transplant 1994; 9:637–641

20. Isner JM, Chokshi SK. Cocaine and vasospasm. N Engl J Med 1989; 321:1604–1606

21. Collis MG. Vascular reactivity to adrenaline and angiotensin-II in the rat perfused mesenteric vasculature. Cardiovasc Res 1975; 9:118–126

22. Lange RA, Cigarroa RG, Yancy CW Jr, Willard JE, Popma JJ, Sills MN et al. Cocaine-induced coronary-artery vasoconstriction N Engl J Med 1989; 321:1557–1562

23. Hebra A, Brown MF, McGeehin K, O'Niell JA Jr, Ross AJ III. Systemic and mesenteric vascular effects of platelet-activating factor and cocaine: *in vivo* effects on a neonatal swine model. Am Surg 1993; 59:50–54

24. Gourgoutis G, Das G. Gastrointestinal manifestations of cocaine addiction. Int J Clin Pharmacol Ther 1993; 32:136–141

25. Rezkalla SH, Mazza JJ, Kloner RA, Tillema V, Chang S. The effect of cocaine on human platelets. Am J Cardiol 1993; 72:243–246

26. Moliterno DJ, Lange RA, Gerard RD, Willard JE, Lackner C, Hillis LD. Influence of intranasal cocaine on plasma constituents associated with endogenous thrombosis and thrombolysis. Am J Med 1994; 96:492–496

27. Jentzen J. Medical complications of cocaine abuse. Am J Clin Pathol 1993; 100:475–476

Potentiation of Warfarin Sodium by Amiodarone-Induced Thyrotoxicosis

KENNETH A. WOEBER, MD, FRCPE
IRVING WARNER, MD
San Francisco, California

THE ANTICOAGULANT EFFECT of warfarin sodium is influenced by several disease states, most notably renal and hepatic dysfunction, and by pharmacokinetic interactions with drugs that either induce or inhibit the hepatic microsomal mixed-function oxidase system.[1] Although thyrotoxicosis has been reported to potentiate the anticoagulant effect of warfarin, necessitating a reduction in dosage,[2–4] this phenomenon is not generally appreciated because the dosage requirements of most other drugs are increased in patients with thyrotoxicosis.[5] We report the case of a patient with severe cardiac disease taking stable maintenance doses of warfarin and amiodarone in whom the emergence of amiodarone-induced thyrotoxicosis was heralded by an abrupt increase in the prothrombin time.

(Woeber KA, Warner I. Potentiation of warfarin sodium by amiodarone-induced thyrotoxicosis. West J Med 1999; 170:49–51)

From the Department of Medicine, University of California, San Francisco (UCSF)/Mount Zion Medical Center, San Francisco, California.

Reprint requests to Kenneth A. Woeber, MD, FRCPE, UCSF/Mount Zion Medical Center, PO Box 1640, San Francisco, CA 94143-1640 (e-mail: woeber@itsa.ucsf.edu).

Report of a Case

The patient, a 73-year-old man, had coronary heart disease, severe left ventricular dysfunction, type 2 diabetes mellitus, systolic hypertension, and hypercholesterolemia. His course had been complicated by recurrent episodes of supraventricular tachycardia that resulted in acute pulmonary edema. Various antiarrhythmic drugs had been used in an attempt to control the episodes of supraventricular tachycardia, but only amiodarone was found to be effective. Accordingly, he had been taking amiodarone, 200 mg a day, for about two years without a recurrence of supraventricular tachycardia. During this period, he had also been taking warfarin to maintain an international normalized ratio (INR) of the prothrombin time of approximately 2.0. His other medications included losartan potassium, metoprolol tartrate, isosorbide mononitrate, furosemide, digoxin, aspirin, pravastatin sodium, and glyburide. On this regimen, he had felt relatively well, and his serum thyrotropin values were normal on numerous occasions, the most recent value being 1.7 mU per liter (normal, 0.4–5.5) in October 1996. He was taking a stable maintenance dose of 3.5 mg of warfarin sodium a day, and the doses of his other medications had not been changed nor had new medications been added.

In February 1997, the patient's INR abruptly increased to 5.5 (verified by repeat analysis), and the dose of warfarin was reduced to 2.5 mg a day (Table 1). In the ensuing two months, the patient noticed increasing effort intolerance, muscle weakness, fatigue, and weight loss without a change in appetite. He had no history of thyroid disease, and thyroperoxidase and thyroglobulin antibodies were absent in serum. He was not taking nonprescription drugs or nutritional supplements.

On examination, he weighed 67 kg (148 lb) and was 71 in tall, with a regular pulse of 90 beats per minute and a blood pressure of 150/70 mm Hg. Eye signs of thyrotoxicosis were absent. The thyroid gland was nontender and normal in size, but firmer than normal and with a finely irregular surface. An S_3 gallop and an apical systolic murmur were present. Breath sounds were decreased at both bases. There was no peripheral edema. The limb-girdle musculature was wasted, and a fine tremor of the hands was present.